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Evaluating the Utility of Electroconvulsive Therapy Cognitive Assessment during and after Electroconvulsive Therapy

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Shanghai Ocean University

2015

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Abstract

Evaluating the Utility of Electroconvulsive Therapy Cognitive Assessment during and after Electroconvulsive Therapy

By: Zixun Ye

Introduction: Electroconvulsive therapy (ECT) is a widespread treatment for major depression, however patients may experience memory loss as a side effect of ECT. A commonly used tool for assessing cognitive function and memory in patients receiving ECT is the Montreal Cognitive Assessment (MoCA). However, it ignores some aspects of the cognitive deficits related to ECT. Electroconvulsive Therapy Cognitive Assessment (ECCA) was developed to address these limitations. The goal of this paper is to perform statistical analysis to investigate the utility of ECCA in detecting cognitive change in patients receiving ECT and determine whether ECCA is a better assessment tool than MoCA.

Methods: Patients with major depression receiving ECT were administrated the ECCA and MoCA at three study phases: baseline (pre-ECT), before the sixth ECT treatment (mid-ECT), and after at least one week from the last treatment (post-ECT). Paired t-tests were used to assess changes in ECCA and MoCA scores between pairs of study phases. Repeated measures analyses were conducted to evaluate the changes of ECCA and MoCA scores across the three study phases, without and with adjustments for confounders, including number of ECT treatment and total number of bilateral lead placement. We examined the association between depression severity and ECCA scores based on two-sample t-tests. We also applied agreement measures to assess the inter-rater reliability of ECCA based on baseline data collected from patients without ECT and healthy controls.

Results: ECCA scores demonstrate a sensible decreasing trend over time, which evidences the cognitive change related to ECT treatments ($P<0.001$). In contrast, MoCA score show significant changes across the three study phases ($P=0.03$) however in the counter-intuitive increasing direction. ECCA scores were significantly different from MoCA scores at mid-ECT and post-ECT phases($P<.001$). Number of ECT treatments and bilateral lead placement are found to have negative impact on ECCA ($P<.05$) while not on MoCA. Lin's concordance correlation coefficient of 0.84 (95% CI: [0.71, 0.92]) suggests good inter-rater reliability of ECCA and further supports its repruducibility in clinical use.

Discussions: ECCA provides an easy, quick, reliable cognitive screening tool for patients undergoing ECT and has good sensitivity to detect memory loss during and after the administration of ECT.

Electroconvulsive therapy Cognitive Assessment: A tool for evaluating during and after the Electroconvulsive Therapy

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1: Introduction

Electroconvulsive therapy (ECT) is a popular way to treat major depression. It has at least two advantages; one is that it is safe, and the other is that it is an effective procedure. However, we may expect to see patients go through memory loss during and after ECT [1]. These side effects are specific to certain cognitive domains not commonly affected in other conditions or diseases [2][3]. Some common tools used for assessing cognitive function and memory in ECT are the Montreal Cognitive Assessment (MoCA) [4] or the Mini-Mental Status Exam (MMSE) [5]. These two instruments are helpful when evaluating Alzheimer's disease and mild cognitive impairment (MCI)[4]. However, they may ignore cognitive deficits when applied to ECT. They may also have gaps in memory evaluation during and after ECT. Electroconvulsive Therapy Cognitive Assessment (ECCA) was built for addressing these limitations and was developed by Dr. Adriana Hermida and other researchers at Emory University in collaboration with researchers at the University of Texas Southwestern Medical Center, Johns Hopkins University, and Duke University School of Medicine [6].

ECCA is a convenient bedside tool that helps ECT practitioners comprised and document bedside cognitive testing. The current assessment contains seven cognitive domains: querying the patients about how they feel about their own memories; asking patients' relatives (usually who accompany the patient) about perception of the patients' cognitive function; testing patients' attention; asking questions about autobiographic memory corroborating with patients' family members; testing the fundamental knowledge and testing patients' recall ability. Each domain was elaborated with the help of

experienced neuropsychologists. The questions don't depend on education level, culture background, they can be commonly used. The list of words used for delayed recall were chosen by a neuropsychologist utilizing a software program that helps with creating three lists with similar levels of difficulty and comparable scores concreteness, number of syllables, imagery, number of letters and similar categories. The ECCA was also developed with the intention to be able to be administrated over the phone in case of patients physically absence. Each domain has its' score, and after the survey, the score in each domain is summed up to make the overall score of the tool. ECCA is not meant to replace extensive neuropsychological tests but it is a tool that included all the elements previously described and could be used as a quick method for the ECT practitioner to guide the treatment course.

The MoCA was developed based on the clinical intuition of *Ziad Nasreddine* regarding domains of impairment commonly encountered in MCI and best adapted to a screening test comparing to that test normal on the MMSE [4]. It consists of a one-page, 30-item memory test that can be administered in ten minutes and consists of eight components: visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation. However MoCA is not developed for the use in the context of ECT specifically. Permission to use the MoCA in the trial was provided from the oficial site.

In the study, three participant groups were recruited: patients with ECT and depression (N=55), patients who meet the criteria for depression but without ECT (N=40),

and healthy normal control (N=41). In the case of the first group, the ECCA and the MoCA were administered by treating physicians and trained mental health professional on three occasions: pre-ECT, before the 6th ECT treatment (mid-ECT), and after the ECT treatment course (post-ECT). The second and third groups were administered both the ECCA and MoCA on one occasion. Patients were recruited from the Emory Wesley Woods Hospital ECT Service and the Emory University Fuqua Center for Late-life Depression in Atlanta, Georgia. The Institutional Review Board of Emory University Hospital approved the study protocol. Depression severity was performed by using the Quick Inventory of Depressive Symptomatology (QIDS-C16) [7]. I obtained the de-identified data from Dr. Hermida and her team and this work is still in progress with collaboration with other universities.

In each assessment session, the patients were required to do the ECCA and MoCA queries. Details for ECCA are as follows: the short-term memory recall task (4 points) involves delayed recall after approximately 5 minutes; temporal orientation (4 points); self memory assessment (4 point); assessment by an informant (4 points) such as a relative; attention tasks including listing month in descending order, combining letter with number in ascending order and patting when hear the specific letter spoken by physicans, and performing a easy arithmetic progression base on physicians required (4 points); autobiographical memory that may require patients to recall what they did in the past (5 points); tests for facutal knowledge (5 points). Also during each survey, physicians note the number of ECT treatments as well as the type of the ECT lead placement, bilateral (BL) lead placement and right unilateral (RUL) lead placement. This study also recruited subjects with depression without ECT and healthy normal subjects. For these two groups

of patients, the tests were conducted once. The collected data can be used to assess the agreement between ECCA and MoCA scores (i.e.whether these two instruments yeild similar outcomes or not). For the inter-rater reliabilty, a group of control subjects did the ECCA tests twice, one week apart, performed by two different raters.

Because ECCA is a new method, some important questions remained to be solved to establish its utility in clinical practice. Investigators were interested in (i) how ECCA assessment captures the cognitive change caused by ECT treatments, and how its performance compared to MoCA; (ii) how the number of ECT treatments and the type of ECT treatments influence the overall scores and sub-domain scores of ECCA and MoCA; (iii) for subjects without ECT treatments (i.e. depression without ECT group, healthy normal group), whether good performance in ECCA assessments agree with good performance in MoCA assessments; (iv) how ECCA and MoCA scores are correlated with depression severity; (v) whether the ECCA instrument has good inter-rater reliability.

The purpose of this thesis project is to address the above questions using thorough statistical analyses. The results will provide useful knowledge and insight for guiding and improving future use of ECCA to capture cognitive changes during and after ECT treatments.

2: Methods

2.1 Demographic Characteristics

The patients were enrolled from Emory Wesley Woods Hospital ECT Service and the Emory University Fuqua Center for Late-life Depression in Atlanta, Georgia. There are three participant groups: depression patients with ECT, depression patients without ECT, and healthy normal subjects. We summarized demographic characteristics in all subjects and compare them among the three participant groups, we got a general demographic information for each group based on Chi-squared test or Fisher exact test for the categorical variable, race, and one-way ANOVA for continuous variables, age and number of education years. We summarized continuous variables by mean ± SD, and categorical variables by count and percentage.

2.2 Evaluating ECCA and MoCA at 3 study phases

In order to check whether test scores changes across different study phases, we first conducted pairwise comparisons of the mean total score of ECCA or MoCA between three pairs of study phases (i.e. mid-ECT vs pre-ECT, post-ECT vs. pre-ECT, and mid-ECT vs. post-ECT) based on paired t tests. Next, we performed repeated measure ANOVA [8][9][10] to investigate whether and how ECCA or MoCA total scores change across the three different study phases while appropriately accounting for within-subject correlations. *Trial*, which indicates the study phase, is the independent variable in the repeated measures ANOVA model [11][12]. To understand the different performance between ECCA and MoCA, we also compared ECCA total score versus MoCA total score separately at each study phases using paired t-tests.

In addition, we examined the score of each question in ECCA because it is of interest to find out which questions contributed to the ECCA scores changes across different study phases. Because the subset questions were answered by "Yes" or "No" , they render binary outcomes.. Hence, we fit repeated measure generized linear models for these longitudinal binary outcomes [13][14].

Moreover, investigators were interested in how the total number of ECT treatments and the type of ECT treatments would affect the total score of MoCA and ECCA and the score for each major cognitive domain. To address this interest, we fit repeated measures linear models on the total and domain scores. The models include the variable *Trail* (which indicates study phase), and the variable that represent number of ECT treatments or the number of some specific type of ECT treatments (e.g. bliateral (BL) lead placements), and possibly their interactions.

2.3 Assessment agreement between ECCA and MoCA and inter-rater reliability of ECCA

For the depression without ECT group and healthy normal control group, both groups had one time test. Investigators set score 23 as a cutoff point to differentiate high cognitive function versus low cognitive function based on either ECCA or MoCA. If the ECCA or MoCA total score was greater than or equal to 23 then the subject was considered to have high cognitive performance otherwise low cognitive performance. We created a 2 by 2 contingency table for the performance classification based on ECCA and MoCA. Because two assessments were given on the same patients, McNemar's test [15] was used

to test homogenity among ECCA and MoCA. The null hypothesis of marginal homogeneity states that the two marginal probabilities for each outcome are the same (i.e, whether the proportion of pairs performing high for ECCA assessment is the same as the proportion of pairs performing high for MoCA assessment).

For the inter-rater reliability of ECCA, the test was conducted by two raters one week away in a control group. Each rater would give score on his/her scale, the purpose was to check if the test would have a comparable outcome for the different practioners. We applied Lin's Concordance Correlation Coefficient [16] to assess, the agreement between the ECCA scores given by different raters on the same subject. The results would indicate inter-rater reliability of ECCA.

2.4 The relation between depression with performance of ECCA assessment

As mentioned above, score 23 was the cutoff point to divide performance of ECCA into high and low. QIDs was an ordinal depression measure: a higher QIDs score means the patient was more depressed. In order to find out the association between ECCA score and depression severity, we compared the QIDs scores between patients with high performance on ECCA and patients with low performance on ECCA based on Wilcoxon rank sum test [17][18]. Rejecting the null hypotheses that, QIDs scores are similar between the two ECCA performance groups would evidence the associationn between ECCA and depression severity.

The significant level set is .05 in our tests and inference. We performed statistical analyses using SAS 9.4 and RStudio Version 0.99.903.

3: Results

3.1 Study Participants and Characteristics

In general, the total number of participant is 136, and there are 3 missing in total in education variable, we treated Unknown in race as missing values and we excluded all the missing values in here and following. Overall, the mean age is 58.99 and mean education year is 15.32, the total number of White patients is 119, total number of African American is 14, with 1 Other race as well as 2 Unknown race. Depression with ECT group consisted 55 patients, however has one missing value in education year, mean age is 57.8 and mean years of education was 15.7. The depression without ECT group comprised of 40 patients. However, it has two missing values in education year. And mean age is 60.3 and mean years of education is 14.8. The healthy control group comprised of 41 patients and mean age is 60.3 and mean years of education is 14.8, which has 3 missing observations in education year. And mean age is 59.4 and mean years of education is 14.8. The mean age ($F_{2,\ 133}$=0.34, MSE=230.1, P=.71), mean years of education ($F_{2,\ 130}$=1.3, MSE=11.1, P=.27), and race (P=.13) were similar throughout the three groups. The overall summary pf demographics and the summary by participant groups are presented in Table 1 in Appendix A.

3.2 Evaluating ECCA and MoCA across Three Study Phases in Depressed Patients Undergoing ECT

Results from tests for each cognitive assessment in 3 time phases can be seen in Figure 1 and Figure 2 in Appendix A. 55 depressed patients underwent the administration of the ECCA and the MoCA during their ECT course. At baseline (pre-ECT), the mean ECCA score is 25.21 (SD=3.21), and the mean MoCA point is 25.75 (SD=2.98). At ECT number 6th (mid-ECT), the mean ECCA score is 22.85 (SD=4.17), and the mean MoCA score is 25.84 (SD=2.97). At the post-ECT phase, the mean ECCA score is 21.75 (SD=4.15), and the mean MoCA score is 26.89 (SD=2.69).By doing the paired t-test in each measurement, ECCA assessment performed statistically significantly different across the three study phases. In contrast, MoCA scores are not statistically significantly different between pre-ECT and mid-ECT. The post-ECT MoCA scores were significantly higher than those at pre-ECT or mid-ECT (P=.016, .014).

3.3 Comparison between ECCA and MoCA in Each Time Phase

Comparison based on paired t-tests show that ECCA and MoCA scores are similar before ECT treatments, while they are statistically significantly different (P<.001) at the study phases, mid-ECT and post-ECT (Figure 3 in Appendix A).

3.4 Comparison in Overall Score of ECCA with MoCA and Memory Domains in 3 Phases

Table 2-1 shows that ECCA scores significantly change across different study phases (P<.001); the changing trend is the ECCA score at mid-ECT is lower than that at pre-ECT and the ECCA score at post-ECT is lower than that at mid-ECT. MoCA scores are also significantly different among the three study phases (P=.03). However, it is shown

that MoCA score increases towards the end of ECT treatment course, which is counter-intuitive.

In addition to overall score, the memory domains showed different association with study phases. Subjective memory assessment (P<.05), assessment by informants (P<.001), attention (P=.03), autobiographic memory (P<.001) and delayed recall (P<.05) were statistically significantly different acorss the three study phases. Comparing post-ECT versus pre-ECT, most of domain scores decrease (except for the fund of knowledge), and assessment by informants part decrease the most (-2). We summerized the results in the Table 2 in Appendix A.

Also, as shown in Table 2-1 and Table 2-2 in Appendix A, in the ECCA model the coefficient estimate for second trial and third trial is negative and statistically significant. While in the MoCA model, the coefficient estimate for second trial and third trial is positive and second trial is not statistically significant. Meanwhile, we used pre-ECT as our reference, so the estimate for intercept is correspond to the pre-ECT estimate. In the total score for ECCA model, the pre-ECT is statistically significant with standard error 0.43 and in the total score for MoCA model, the pre-ECT is statistically significant with standard error 0.40.

After knowing which domains mattered, investigators wanted to know which questions in each domain would statistically significantly impacted by numbers of ECT treatments. Now we looking into domains those are statistically significantly impacted by

number of ECT treatment. And for each domain, they are all binary outcome, that is, the outcome is either "YES" or "NO". So, in order to address the problem, we built generalized linear models, which each subset question is outcome and times of ECT treatment is predictor. Basically, we wanted to test how the times of ECT treatment affect subset questions, and we had 3 trials, and for each patient, they were correlated when consider the data in longitudinal term. Then we did repeated measure based on the model. After sorting out domains which had statistically significantly change within times of ECT treatment, we performed the same repeated longitudinal measure on their subset questions to determine which subset questions in each domain had statistically significant effect with times of ECT treatment. The outcomes show that for those domains, they all have some sub-questions have significantly impact on the overall change. In conclusion, for the subject domain, response changes in question 1(P=.03) is statistically significant; In the informant part, response changes in question 1 (P<.001), 3 (P<.05), and 4 (P<.001) are statistically significant; attention has question 2 (P<.05) response to which changes statistically significantly; for the autobiographical memory, response changes in question 4 (P<.05), and question 5 (P<.05) are statistically significant; for the recall, response changes in question 2 (P=.01), and question 4 (P<.05) are statistically significant. Meanwhile, when performed the same test on those domains that total score is already not significant (Orientation and Fund of Knowledge), the outcome show that none of them have subset that are statistically significant (Table 3 in Appendix A).

3.5 Effect of Total Number of ECT Treatments on ECCA and MoCA and Major Cognitive Domains

First, we analyzed the models that include the interaction term between study phase and the number of ECT treatments. In all models, this interaction term is not statistically significant (Table 10 in Appendix B). Thus we removed the interaction term from the models and only include study phase and number of ECT treatments as the predictors.

The total number of ECT treatments have no statistically significantly impact on total score of MoCA (P=.58). However it has statistically significantly effect on total score of ECCA (P=.03). A decreasing trend exists between total score within either MoCA or ECCA with the increasing amount of treatment times.

For memory cognitive domains, the total number of treatments have statistically significantly effect on subjective memory (P=.02), attention (P=.02), and autobiographical (P<.05). The p-value for them shown below (Table 4 in Appendix A)

3.6 Effect of Total Number of Bilateral (BL) Placements on ECCA and MoCA and Major Cognitive Domains

We investigated the impact of total number of BL placements on ECCA and MoCA in the same way as we investigated the impact of total number of ECT treatments.

We find that the total number of BL had no statistically significantly impact on total score of MoCA (P=.29). However it had a statistically significantly effect on total score of ECCA (P<.05). However the decreasing trend existed between total score within either MoCA or ECCA with the increasing amount of BL placement times

Besides, number of BL placements had statistically significant effect in subject memory (P<.001) performance and objective by informant (P<.001) (Table 5 in Appendix A). In these two cognitive domains, the more BL number was, the less the score was in either major domains.

3.7 Internal Consistency in Depressed without ECT group and Healthy Normal group

In the analysis, we set score 23 as the cutoff to determine the performance status of ECCA or MoCA (i.e. high performance or low performance). The 2 by 2 table contigency table for MoCA versus ECCA performance status in depression patients without ECT is given by Table 6 in Appendix A, the Kappa coefficient estimated based on this table is .68 [.35, 1.0], which shows a modest agreement between ECCA and MoCA. There is no statistically significant difference in performance status between ECCA and MoCA (P=.56). These results suggest that, patients with depression but without ECT who have lower score in ECCA tend to have lower score in MoCA. In healthy control group, the agreement in performance status between ECCA and MoCA is perfect (Table 7 in Appendix A).

In order to figure out the relation between depression and performance of ECCA in the depression without ECT group, we conducted non-parametric analysis. Wilcoxon two-sample test [19] yields a two sided p value of .05, one sided p value of .03. This suggests that patients with high performance in ECCA tends to have lower depression score than

those with low performance in ECCA. This indicates a significant association between depression severity and ECCA performance (Figure 4 in Appendix A).

3.8 Inter-rater Reliability

Two physicians (raters) performed ECCA test on the same patients one week apart. The estimate for Lin's concordance correlation coefficient of the ECCA scores from the two raters is .84 with 95% confidence interval [0.71, 0.92]. This indicates good inter-rater agreement/reliability of ECCA (Figure 5 in Appendix A).

4: Discussions and Concluding Remarks

ECCA is an effective, accurate, easy-operated and quick procedure. The tool was made to evaluate certain cognitive domains such as orientation, attention, executive function, and delayed verbal recall. The method also provides information that include the informant, i.e, confirmation from others (usually relatives), self-reported perceived cognitive difficulties (subjective), and ability to recall any daily life material (autobiographic).

Nowadays the challenge to all the physicians who conduct ECT is the need of a reliable as well as quick and efficient tool to assess the memory loss during the treatment. Because ECT could cause autobiographic memory loss [20][21] attention deficits and subjective memory impairment [22] (the patient's perception of his or her cognitive capacity) it si vital to assess all of these domains in patients undergoing ECT [23].

The ECCA is a practical tool that can capture cognitive impirment during ECT, it can be administrated in less than 10 minutes and it is suitable for clinical settings. Clinical practice and collected data demonstrated ECCA is a valid tool that can be repeatedly administer as well as yields objectives outcomes [24][25]. This data is supported by the ECCA domain of subjective memory, informant-based section, attention, autobiographical memory and delayed recall, which showed statistical significance over the period of ECT treatments.

The ECCA was also effective in evaluating cognitive status in depressed patients who were not experiencing ECT and healthy normal controls. This displays the utility of the ECCA in establishing baseline cognition pre-ECT and cognitive changes during and after the ECT course.

4.1 ECCA Versus MoCA on Identifying Cognitive Change during ECT

ECCA demonstrated high sensitivity in detecting cognitive impairment during ECT treatment comparing to MoCA. In the depression with ECT group, as time goes on, the ECCA total score is decreasing while MoCA total score does not. In this case, the decreasing in total ECCA score actually supports the fact that patients may experience some decline in cognitive function during ECT. Also, while comparing the total score between each time point in either assessment, ECCA showed statistically significant different in 3 test period while MoCA only showed statistically significant different between pre-ECT with post-ECT and mid-ECT with post-ECT. In addition, the overall

trend of MoCA's score is increasing, while p-value is significant, showing a contracting result. Therefore, when using ECCA, we could observe more statistically significant reduction in memory as we expected than using MoCA. The comparison between two assessments in each test phase also illustrated that when ECT treatment undergoing, performance of assessments has significantly statistical different at second and last session. Which includes two assessment have different sensitivity when detecting memory loss. Thus cognitive deficits during and after ECT treatment could be detected by using ECCA.

4.2 Evaluation for Major Domains

The ECCA assessment is a questionnaire with queries grouped by domains. In order to evaluate whether domains are sensitive to a 3 phases test, we did a repeated measure analysis and the result displayed subjective memory assessment, assessment by informants, attention, autobiographic memory and delayed recall were more sensitive in capturing cognitive decline. Orientation domain score remained the same during the treatment course. Patients tend to have constant memory of date, year and where he/she is because these can be reminded before the test begin and all these questions can be memorized without effort. An increasing trend for the fund of knowledge domain was noticed. One explanatory factor for that is in each session, patients were asked about exactly same questions. Especially for the fund of knowledge part, the questions were all about well kown information. Physicians would not tell the answers to patients after quizzes, however there may exist a learning effect during testing for these constant facts.

After we found out how domains were sensitive to cognitive change, we also wanted to know what questions under each domain were more sensitive. After analysis, we found out which domains were statistically significantly different through the test. Each domain had specific questions that were statistically significantly different through the test too. For domains that were not statistically significantly different through the test, none of the quizzes of them were statistically significantly different either. Hence, some questions might be omitted if not clinically significant. However the fact that some aspects remain stable could provide important information for the practitioner.

4.3 Impact of Total Number of ECT Treatments

In the hypothesis, investigators wanted to know how the total number of ECT treatments would affect the performance of the assessment. At first, we built a model with test phase and total number of ECT treatments interaction. However, we did not see any statistically significant change in the interaction term, it may due to the lower power of the data. Hence, we removed interaction term and looked into total number of ECT only. Results showed total number of ECT treatments has statistically significant impact on ECCA while not statistically significant impact on MoCA. Which represents ECCA is a better assessment for capturing cognitive change during ECT treatment. For the domains of the ECCA test, subjective memory, attention and autobiographical were statistically significant impacted by number of treatment. Results displayed that most of domains' score would decrease through the test when only consider of total number of ECT treatments (both RUL and BL placements) (Table 21-29 in Appendix B).

4.4 Impact of Total Number of Bilateral Lead Placements

Bilateral ECT has been associated with more memory loss compared with unilateral lead placement. Therefore, in the hypothesis, investigator wanted to know how the total number of BL would affect the performance of the assessment. At first, we built a model with test phase and total number of ECT treatment interaction. However, we did not see any statistically significant change in the interaction term except in MoCA model, it may due to the lower power of the data. Hence, we removed interaction term and looked into total number of BL only. Results showed total number of BL has statistically significant impact on ECCA while not statistically significant impact on MoCA. Which represents ECCA may be a better assessment for capturing cognitive change with BL placement. BL placement also had statistically significant impact on subjective, informant and autobiographical memory. In conclusion, these sections are more sensitive to the impact of BL placement. Outcome demonstrated that most of domains' score would decrease through the test when only consider of BL placement (Table 30-38 in Appendix B). We expect that patients who got more BL placements, had worse performance in answering those domains. Future analysis need to be done when patients perform badly in those sections, whether patients received more BL placement electrode placement.

4.5 Internal Consistency and Inter-rater Reliability

The analysis of inter-rater reliability evaluation in healthy normal group demonstrated that ECCA has a relative high internal consistency and is a reproducible assessment. Without ECT treatment interference, ECCA assessment still performs well in the depression and normal group. In the depression group, QIDs score is a measurement of

scale of depression, and we already divided participants' test score into high and low. Result yielded that participants performed worse in the test had higher depression, performed better in the test had lower depression. The negative association between depression with performance may represent the relation between cognitive function and mental health status (depression) however future work needed to be done. Besides, the moderate agreement in depressed group suggested without ECT treatment, performance is similar among individual. Which suggested ECCA is a specific tool to detect memory loss caused by ECT treatment compared to MoCA.

In addition, the perfect match of two raters in the healthy normal group demonstrated that the ECCA has a high degree of agreement or concordance between raters.

4.6 Conclusions

The results of this analysis display that ECCA is a better cognitive screening tool than MoCA for patients undergoing ECT. After a course of ECT treatment, the results of statistical significant reduction in total score of ECCA supported ECCA is a sensitive assessment in capturing the cognitive change during the treatment. In addition, some of domains were more sensitive which supports that ECCA has an appropriate questions design. Moreover, the validity and inter-rater reliability results of the analysis demonstrated ECCA is a consistent, applicable, practicable and reproducible tool.

4.7 Strengths and Limitations

ECCA test can be done in less than 10 minutes, which is an efficient test as well as a reliable test, because it can easily capture cognitive change and would yield same results on the same patients even conducted by different clinicians. Also, this analysis included data from depressed patients who underwent ECT treatment, depressed patients not underwent ECT treatment and healthy control, with similar education background, age and race, which provides norms for the ECCA. Despite these strengths, there are also some limitations to the analysis. For example, the data had lower power which failed us to interpret interaction effect of total number of ECT treatment with test phase, of total number of BL placement with test phase. If the collected data had relative higher power, it may allow for further interpretability of results.

4.8 Recommendations

These results can be useful for the future studies regarding how and whether ECT treatment has more side-effects on short-term memory or long-term memory or both. Also, with the help of these outcome, investigators can modify the method by replacing insensitive sub-questions with sensitive ones, However, those new questions need to be tested too. Additionally, the timing for patients underwent the last treatment varies. Therefore, the period between mid-ECT with post-ECT is different for each patient. The further analysis of relation between the period with memory loss need to be done. In addition, how performance of patients relate to the sections could be used to predict the number of ECT treatment or times of BL placements is required for a further analysis.

References

[1]. Gardner BK, O'Connor DW. A review of the cognitive effects of electroconvulsive therapy in older adults. The journal of ECT 2008;24:68-80.

[2]. Kho KH, VanVreeswijk MF, Murre JM. A retrospective controlled study into memory complaints reported by depressed patients after treatment with electroconvulsive therapy and pharmacotherapy or pharmacotherapy only. The journal of ECT 2006;22:199-205.

[3]. Fujita A, Nakaaki S, Segawa K, et al. Memory, attention, and executive functions before and after sine and pulse wave electroconvulsive therapies for treatment-resistant major depression. The journal of ECT 2006;22:107-12.

[4]. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. Journal of the American Geriatrics Society 2005;53:695-9.

[5]. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.

[6]. Hermida, AP; Henderson, S; Tang, Y; Galendez, G; Goldstein, F; Loring, D; McClintock, SM; Weiner, R; Husain, M; Reti, I; Maixner, D; McDonald, WM Validation of a Brief Cognitive Tool (ECA) Designed Specifically for Use During and After Electroconvulsive Therapy. 2015 ISEN abstracts, Journal of ECT Volume 31(3) pgs e32-e39 September 2015 ISSN: 1095-0680

[7]. http://www.ids-qids.org/ date accessed 3/31/2017

[8]. Diggle, P. J., Liang, K., and Zeger, S. L. (1994), Analysis of Longitudinal Data, Oxford: Clarendon Press, 253pp.

[9]. Johnson, R. A. and Wichern, D. W. (2002), Applied Multivariate Statistical Analysis, Fifth Edition, Upper Saddle River, NJ : Prentice Hall, 767pp.

[10]. Lindsey, J.K. (1993), Models for Repeated Measurements, Oxford: Clarendon Press, 413pp.

[11]. Littell, R. C., Milliken, G. A., Stroup, W. W., and Wolfinger, R. D. (1996), SAS® System for Mixed Models, Cary, NC: SAS Institute, Inc., 633pp.

[12]. http://support.sas.com/documentation/cdl/en/statug/63033/HTML/default/viewer.htm#statug_mixed_sect008.htm/ date accessed 11/20/2016

[13]. Agresti, A. Categorical Data Analysis (1990).New York: Wiley.

[14]. Neter J., Wasserman J. and Kutner M. (1990). Applied Linear Statistical Models. Boston: Irwin.

[15]. McNemar, Quinn (June 18, 1947). "Note on the sampling error of the difference between correlated proportions or percentages". Psychometrika. 12 (2): 153–157.

[16]. Lin, Lawrence I-Kuei. March, 1989. 'A Concordance Correlation Coefficient to Evaluate Reproducibility.Biometrics 45, 255-268.

[17]. https://onlinecourses.science.psu.edu/stat464/node/36 / date accessed 01/29/2017

[18]. Corder, G.W. ; Foreman, D.I. (2014). Nonparametric Statistics: A Step-by-Step Approach. Wiley

[19]. http://www.stat.purdue.edu/~tqin/system101/method/method_wilcoxon_rank_sum_sas.htm date accessed 01/29/2017

[20]. Fraser LM, O'Carroll RE, Ebmeier KP. The effect of electroconvulsive therapy on autobiographical memory: a systematic review. The journal of ECT 2008;24:10-7.

[21]. Sackeim HA, Prudic J, Fuller R, Keilp J, Lavori PW, Olfson M. The Cognitive Effects of Electroconvulsive Therapy in Community Settings.Neuropsychopharmacology 2007;32:244-54.

[22]. Prudic J, Peyser S, Sackeim HA. Subjective memory complaints: a review of patient self-assessment of memory after electroconvulsive therapy. The journal of ECT 2000;16:121-32.

[23]. Coleman EA, Sackeim HA, Prudic J, Devanand DP, McElhiney MC, Moody BJ. Subjective memory complaints prior to and following electroconvulsive therapy. Biological psychiatry 1996;39:346-56.

[24]. Cabrera-Nguyen P. Author Guidelines for Reporting Scale Development and Validation Results in the Journal of the Society for Social Work and Research. Journal of the Society for Social Work and Research 2010;1:99-103.

[25]. Bland JM, Altman DG. Statistics Notes: Validating scales and indexes. BMJ (Clinical research ed) 2002;324:606-7.

Appendix A: Tables and figures

Table 1: Subject demographics

	Overall	Dep w/ ECT	Dep w/o ECT	Healthy Control	p-value
	N=136	N=55	N=40	N=41	
Age(years)	59.0±15.09	57.8±17.06	60.3±12.35	59.4±14.94	0.71
Race					0.13
White	119(88.81%)	52(94.55%)	35(87.5%)	32(82.05%)	
African American	14(10.45%)	3(5.45%)	4(10.0%)	7(17.95%)	
Other	1(0.75%)	0(0%)	1(2.5%)	0(0%)	
Education(years)	15.3±3.34	15.7±2.66	14.8±2.86	14.8±2.86	0.27

Table 2: Repeated Measure Analysis in ECCA and MoCA

ECT Patient (n=55)

Test Name	Pre-ECT Visit	ECT 6 Visit	Post-ECT Visit	P-value#
Orientation	3.9±0.04	3.9±0.04	3.9±0.04	0.94
Subjective	2.9±0.14	2.9±0.15	2.4±0.16	<.05*
Informant	3.3±0.12	2.8±0.15	1.9±0.18	<.001*
Attention	3.3±0.13	3.0±0.15	2.9±0.15	0.03*
Autobiographic	4.5±0.11	3.9±0.16	3.5±0.19	<.001*
Fund of Knowledge	4.6±0.10	4.6±0.08	4.7±0.07	0.23
Recall	2.7±0.17	2.1±0.20	2.2±0.18	<.05*
Total ECCA Score	25.2±3.21	22.9±4.17	21.7±4.15	<.001*
Total MOCA Score	25.7±2.98	25.8±2.97	26.9±2.69	0.03*

The parametric p-value is calculated by ANOVA for numerical covariates; * means statistically significant.

Table 2-1: Solution for Fixed Effect for Total Score of ECCA

Effect	Estimate	Standard Error	P-value*
Intercept	25.2	0.43	<.001*
Mid-ECT	-2.4	0.59	<.001*
Post-ECT	-3.5	0.62	<.001*
Pre-ECT	0		

* means statistically significant.

Table 2-2: Solution for Fixed Effect for Total Score of MoCA

Effect	Estimate	Standard Error	P-value*
Intercept	25.7	0.40	<.001*
Mid-ECT	0.1	0.38	0.81
Post-ECT	1.1	0.46	0.02*
Pre-ECT	0		

* means statistically significant.

Table 3: Repeated Measure Analysis in subset question in ECCA

Domains	Pre-ECT Visit N(%)[+]	ECT 6 Visit N(%)[+]	Post-ECT Visit N(%)[+]	P-value
Subjective				
Question 1	31(56.36%)	26(47.27%)	38(69.09%)	0.03*
Question 2	5(9.09%)	10(18.18%)	12(21.82)	0.18
Question 3	11(20.00%)	10(18.18%)	16(29.09%)	0.24
Question 4	12(25.45%)	19(34.55%)	24(43.64)	0.10
Informant				
Question 1	18(32.73%)	30(54.55%)	42(76.36%)	<.001*
Question 2	7(12.73%)	8(14.55%)	14(25.45%)	0.11
Question 3	7(12.73%)	10(18.18%)	22(40.00%)	<.05*
Question 4	5(9.09%)	21(38.18%)	31(56.36%)	<.001*
Attention				
Question 1	49(89.09%)	50(90.91%)	44(80.00%)	0.10
Question 2	48(81.82%)	31(56.36%)	33(60.00%)	<.05*
Question 3	52(94.55%)	46(83.64%)	49(89.09%)	0.13
Question 4	36(65.45%)	35(63.64%)	36(65.45%)	0.94
Autobiographical				
Question 1	49(89.09%)	44(80.00%)	43(78.18%)	0.24
Question 2	48(87.27%)	44(80.00%)	42(76.36%)	0.27
Question 3	50(90.91%)	46(83.64%)	43(78.18%)	0.18
Question 4	49(89.09%)	40(72.73%)	30(50.44%)	<.05*
Question 5	49(89.09%)	41(74.55%)	34(61.82%)	<.05*
Recall				
Question 1	39(70.91%)	28(50.91%)	28(50.91%)	0.07
Question 2	38(69.09%)	21(38.18%)	34(61.82%)	0.01*
Question 3	25(45.45%)	28(50.91%)	26(47.27%)	0.84
Question 4	45(81.82%)	37(67.27%)	33(60%)	<.05*
Orientation				
Question 1	55(100%)	55(100%)	55(100%)	N/A
Question 2	55(100%)	55(100%)	55(100%)	N/A
Question 3	54(98.18%)	52(94.55%)	52(94.55%)	0.45
Question 4	55(100%)	55(100%)	55(100%)	N/A
Fund of Knowledge				
Question 1	55(100%)	55(100%)	55(100%)	N/A
Question 2	46(83.64%)	47(85.45%)	50(90.91%)	0.34
Queston 3	53(96.36%)	53(96.36%)	54(98.18%)	0.51
Question 4	54(98.18%)	52(94.55%)	53(96.36%)	0.22
Question 5	45(81.82%)	45(81.82%)	48(87.27%)	0.22

[+] means number of YES in each question; * means statistically significant.

Table 4: Type 3 P-value for Variables interact without Total number of ECT

Variables	Test Phase	Total number of ECT
Total Score of ECCA	<.001*	0.03*
Total Score of MoCA	0.03*	0.58
Orientation	0.94	0.11
Subjective	<.001*	0.02*
Informant	<.001*	0.44
Attention	0.50	0.02*
Autobiographical	0.03*	0.04*
Fund of Knowledge	0.23	0.97
Recall	0.05	0.63

* means statistically significant.

Table 5: Type 3 P-value for Variables interact without Total number of BL

Variables	Test Phase	Total number of BL
Total Score of ECCA	<.001*	<0.05*
Total Score of MoCA	0.03*	0.29
Orientation	0.94	0.87
Subjective	0.03*	<.001*
Informant	<.001*	<.001*
Attention	0.03*	0.24
Autobiographical	<.001	0.03*
Fund of Knowledge	0.23	0.67
Recall	<.05*	0.07

* means statistically significant.

Table 6: 2 by 2 table for performance of MoCA and ECCA in depressed without ECT group (Kappa=.68 [.35, 1.0])

Performance of ECCA / Performance of MoCA	Low	High	Total
Low	4	1	5
High	2	33	35
Total	6	34	40

Table 7: 2 by 2 table for performance of MoCA and ECCA in healthy normal control group (Kappa=1 [1.0, 1.0])

Performance of ECCA / Performance of MoCA	Low	High	Total
Low	0	0	0
High	0	41	41
Total	0	41	41

Figure 1: Comparison of ECCA Score in 3 time periods

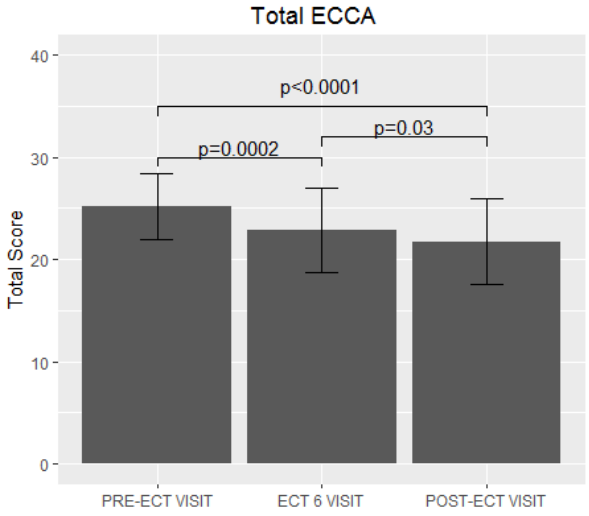


Figure 2: Comparison of MoCA Score in 3 time periods

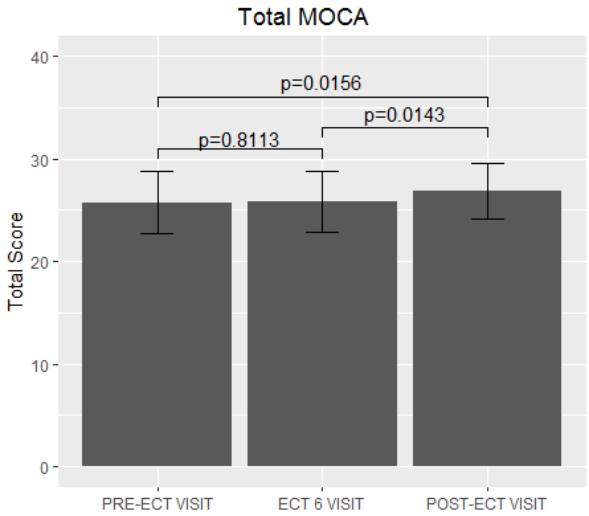


Figure 3: Pre, Mid and Post-ECT Comparison between ECCA and MoCA Scores

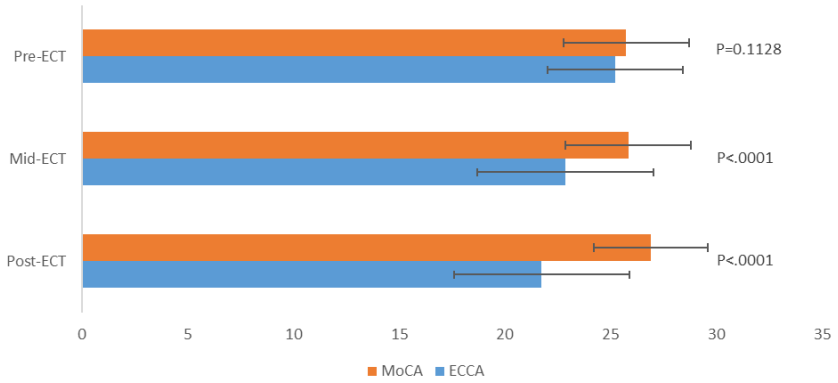


Figure 4: Comparison of depression score between ECCA with high score and ECCA with low score using nonparametric test (P=.05)

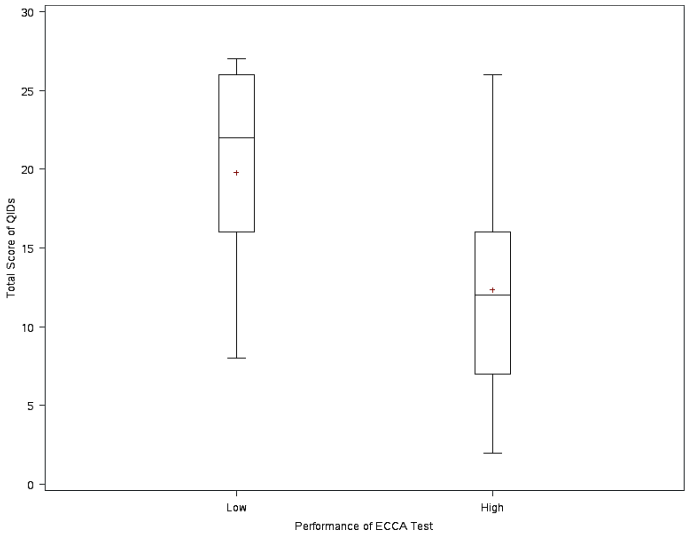
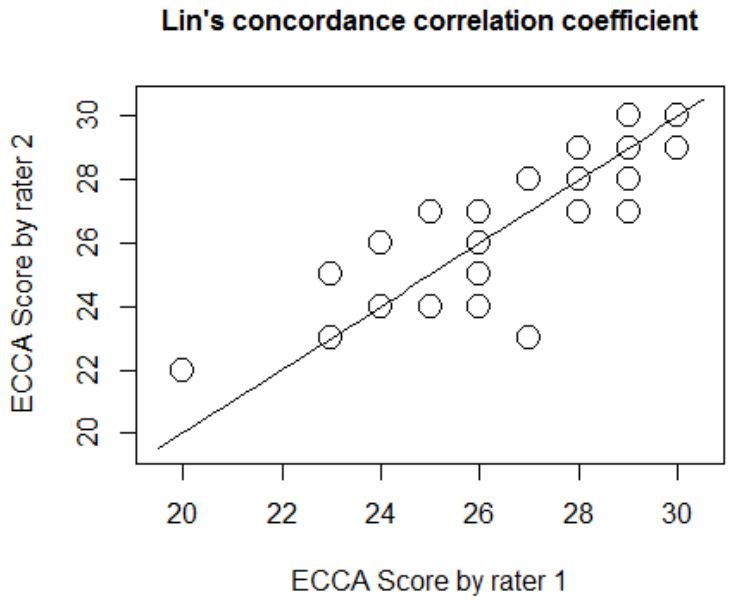


Figure 5: Lin's concordance correlation coefficient



Appendix B: Tables

Table 1: Solution for Fixed Effects of Total Score of ECCA with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	25.5	1.50	<.001*
Mid-ECT VS Pre-ECT	-0.8	2.08	0.71
Post-ECT VS Pre-ECT	-2.7	2.19	0.23
Total number of ECT VS Pre-ECT	-0.2	0.14	0.12
Mid-ECT*Total number of ECT VS Pre-ECT	-0.2	0.20	0.43
Post-ECT*Total number of ECT VS Pre-ECT	-0.1	0.21	0.71

* means statistically significant.

Table 2: Solution for Fixed Effects of Total Score of MoCA with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	27.2	1.41	<.001*
Mid-ECT VS Pre-ECT	-2.8	1.28	0.03
Post-ECT VS Pre-ECT	0.2	1.62	0.90
Total number of ECT VS Pre-ECT	-0.2	0.13	0.26
Mid-ECT*Total number of ECT VS Pre-ECT	0.3	0.12	0.02*
Post-ECT*Total number of ECT	0.1	0.15	0.55

* means statistically significant.

Table 3: Solution for Fixed Effects of Total Score of Orientation with number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	3.9	0.14	<.001*
Mid-ECT VS Pre-ECT	-0.1	0.19	0.53
Post-ECT VS Pre-ECT	-0.2	0.19	0.35
Total number of ECT	0.002	0.01	0.86
Mid-ECT*Total number of ECT VS Pre-ECT	0.01	0.02	0.58
Post-ECT*Total number of ECT VS Pre-ECT	0.02	0.02	0.38

* means statistically significant.

Table 4: Solution for Fixed Effects of Total Score of Subjective with number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	3.9	0.47	<.001*
Mid-ECT VS Pre-ECT	-0.1	0.58	0.92
Post-ECT VS Pre-ECT	-0.8	0.60	0.20
Total number of ECT VS Pre-ECT	-0.1	0.05	0.04
Mid-ECT*Total number of ECT VS Pre-ECT	0.006	0.05	0.91
Post-ECT*Total number of ECT VS Pre-ECT	0.03	0.06	0.61

* means statistically significant.

Table 5: Solution for Fixed Effects of Total Score of Informant with number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	3.5	0.44	<.001*
Mid-ECT VS Pre-ECT	-0.7	0.62	0.26
Post-ECT VS Pre-ECT	-0.7	0.73	0.36
Total number of ECT VS Pre-ECT	-0.02	0.04	0.70
Mid-ECT*Total number of ECT VS Pre-ECT	0.02	0.06	0.79
Post-ECT*Total number of ECT VS Pre-ECT	-0.08	0.07	0.28

* means statistically significant.

Table 6: Solution for Fixed Effects of Total Score of Attention with number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	4.3	0.45	<.001*
Mid-ECT VS Pre-ECT	-0.5	0.53	0.33
Post-ECT VS Pre-ECT	-0.7	0.67	0.28
Total number of ECT VS Pre-ECT	-0.09	0.04	0.04
Mid-ECT*Total number of ECT VS Pre-ECT	0.01	0.05	0.77
Post-ECT*Total number of ECT VS Pre-ECT	0.03	0.06	0.63

* means statistically significant.

Table 7: Solution for Fixed Effects of Total Score of Autobiographical with number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	5.1	0.39	<.001*
Mid-ECT VS Pre-ECT	-0.04	0.59	0.94
Post-ECT VS Pre-ECT	-1.27	0.79	0.12
Total number of ECT	-0.06	0.04	0.10
Mid-ECT*Total number of ECT VS Pre-ECT	-0.05	0.06	0.38
Post-ECT*Total number of ECT VS Pre-ECT	0.03	0.08	0.67

* means statistically significant.

Table 8: Solution for Fixed Effects of Total Score of Fund of Knowledge with number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	2.2	0.61	<.001*
Mid-ECT VS Pre-ECT	0.7	0.90	0.43
Post-ECT VS Pre-ECT	0.4	0.78	0.65
Total number of ECT VS Pre-ECT	0.04	0.06	0.44
Mid-ECT*Total number of ECT VS Pre-ECT	-0.1	0.09	0.13
Post-ECT*Total number of ECT VS Pre-ECT	-0.08	0.07	0.27

* means statistically significant.

Table 9: Solution for Fixed Effects of Total Score of Recall with number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	5.1	0.39	<.001*
Mid-ECT VS Pre-ECT	-0.04	0.59	0.95
Post-ECT VS Pre-ECT	-1.3	0.79	0.12
Total number of ECT	-0.06	0.04	0.10
Mid-ECT*Total number of ECT VS Pre-ECT	-0.05	0.06	0.38
Post-ECT*Total number of ECT VS Pre-ECT	0.03	0.08	0.67

* means statistically significant.

Table 10: Type 3 P-value for Variables interact with Total number of ECT

Variables	Test Phase	Total number of ECT	Variable*Total number of ECT
Total Score of ECCA	0.41	0.02*	0.72
Total Score of MoCA	0.04*	0.81	0.06
Orientation	0.64	0.12	0.67
Subjective	0.30	0.04*	0.85
Informant	0.52	0.33	0.24
Attention	0.50	0.03*	0.89
Autobiographical	0.17	0.07	0.36
Fund of Knowledge	0.83	0.74	0.55
Recall	0.73	0.52	0.30

* means statistically significant.

Table 11: Solution for Fixed Effects of Total Score of ECCA with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	25.8	0.53	<.001*
Mid-ECT VS Pre-ECT	-2.1	0.74	0.006*
Post-ECT VS Pre-ECT	-2.9	0.76	<.001*
BL VS Pre-ECT	-0.2	0.11	0.05
Mid-ECT*BL VS Pre-ECT	-0.1	0.15	0.56
Post-ECT*Total number of ECT VS Pre-ECT	-0.2	0.16	0.20

* means statistically significant

Table 12: Solution for Fixed Effects of Total Score of MoCA with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	25.9	0.50	<.001*
Mid-ECT VS Pre-ECT	-0.4	0.46	0.38
Post-ECT VS Pre-ECT	1.6	0.57	0.01*
BL VS Pre-ECT	-0.03	0.10	0.71
Mid-ECT*BL VS Pre-ECT	0.2	0.09	0.08
Post-ECT*Total number of ECT VS Pre-ECT	-0.1	0.11	0.28

* means statistically significant.

Table 13: Solution for Fixed Effects of Total Score of Orientation with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	3.9	0.05	<.001*
Mid-ECT VS Pre-ECT	-0.04	0.07	0.61
Post-ECT VS Pre-ECT	-0.0008	0.07	0.99
BL VS Pre-ECT	0.001	0.01	0.93
Mid-ECT*BL VS Pre-ECT	0.01	0.01	0.68
Post-ECT*Total number of ECT VS Pre-ECT	-0.01	0.01	0.68

* means statistically significant.

Table 14: Solution for Fixed Effects of Total Score of Subjective with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	3.1	0.16	<.001*
Mid-ECT VS Pre-ECT	0.07	0.20	0.7
Post-ECT VS Pre-ECT	-0.4	0.21	0.07
BL VS Pre-ECT	-0.09	0.03	0.01*
Mid-ECT*BL VS Pre-ECT	-0.02	0.04	0.56
Post-ECT*Total number of ECT VS Pre-ECT	-0.03	0.04	0.48

* means statistically significant

Table 15: Solution for Fixed Effects of Total Score of Informant with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	3.5	0.15	<.001*
Mid-ECT VS Pre-ECT	-0.6	0.22	0.005*
Post-ECT VS Pre-ECT	-1.2	0.26	<.001*
BL VS Pre-ECT	-0.07	0.03	0.02*
Mid-ECT*BL VS Pre-ECT	0.03	0.04	0.47
Post-ECT*Total number of ECT VS Pre-ECT	-0.07	0.05	0.17

* means statistically significant.

Table 16: Solution for Fixed Effects of Total Score of Attention with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	3.4	0.17	<.001*
Mid-ECT VS Pre-ECT	-0.5	0.19	0.02*
Post-ECT VS Pre-ECT	-0.3	0.24	0.15
BL VS Pre-ECT	-0.02	0.03	0.52
Mid-ECT*BL VS Pre-ECT	0.03	0.04	0.49
Post-ECT*Total number of ECT VS Pre-ECT	-0.02	0.05	0.61

* means statistically significant.

Table 17: Solution for Fixed Effects of Total Score of Autobiographical with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	4.6	0.14	<.001*
Mid-ECT VS Pre-ECT	-0.37	0.21	0.08
Post-ECT VS Pre-ECT	-0.90	0.28	<.001*
BL VS Pre-ECT	-0.03	0.03	0.23
Mid-ECT*BL VS Pre-ECT	-0.06	0.04	0.18
Post-ECT*Total number of ECT VS Pre-ECT	-0.02	0.06	0.78

* means statistically significant.

Table 18: Solution for Fixed Effects of Total Score of Fund of Knowledge with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	4.6	0.12	<.001*
Mid-ECT VS Pre-ECT	0.03	0.09	0.77
Post-ECT VS Pre-ECT	0.1	0.11	0.34
BL VS Pre-ECT	0.01	0.02	0.68
Mid-ECT*BL VS Pre-ECT	-0.02	0.02	0.40
Post-ECT*Total number of ECT VS Pre-ECT	<.01	0.02	0.99

* means statistically significant.

Table 19: Solution for Fixed Effects of Total Score of Recall with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	2.7	0.22	<.001*
Mid-ECT VS Pre-ECT	-0.4	0.32	0.19
Post-ECT VS Pre-ECT	-0.2	0.27	0.45
BL VS Pre-ECT	-0.01	0.04	0.81
Mid-ECT*BL VS Pre-ECT	-0.06	0.07	0.39
Post-ECT*Total number of ECT VS Pre-ECT	-0.09	0.06	0.11

* means statistically significant.

Table 20: Type 3 P-value for Variables interact with Total number of BL

Variables	Test Phase	Total number of BL	Variable*Total number of BL
Total Score of ECCA	<.05*	<.05*	0.42
Total Score of MoCA	<.001*	0.76	0.01*
Orientation	0.80	0.87	0.59
Subjective	0.04	<.001*	0.76
Informant	<.001*	<.001*	<.001*
Attention	0.06	0.43	0.43
Autobiographical	0.01*	0.03*	0.33
Fund of Knowledge	0.59	0.77	0.57
Recall	0.42	0.05	0.28

* means statistically significant.

Table 21: Solution for Fixed Effects of Total Score of ECCA with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	28.0	1.29	<.001*
Mid-ECT VS Pre-ECT	-2.4	0.59	<.001*
Post-ECT VS Pre-ECT	-3.5	0.62	<.001*
Total number of ECT VS Pre-ECT	-0.3	0.12	0.03*

* means statistically significant.

Table 22: Solution for Fixed Effects of Total Score of MoCA with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	26.3	1.09	<.001*
Mid-ECT VS Pre-ECT	0.1	0.38	0.81
Post-ECT VS Pre-ECT	1.1	0.46	0.02*
Total number of ECT VS Pre-ECT	-0.1	0.10	0.58

* means statistically significant.

Table 23: Solution for Fixed Effects of Total Score of Orientation with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	3.8	0.08	<.001*
Mid-ECT VS Pre-ECT	-0.02	0.05	0.74
Post-ECT VS Pre-ECT	-0.02	0.05	0.74
Total number of ECT VS Pre-ECT	0.01	0.01	0.11

* means statistically significant.

Table 24: Solution for Fixed Effects of Total Score of Subjective with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	3.8	0.41	<.001*
Mid-ECT VS Pre-ECT	<.001	0.16	1.00
Post-ECT VS Pre-ECT	-0.5	0.17	<.05*
Total number of ECT VS Pre-ECT	-0.1	0.04	0.02*

* means statistically significant.

Table 25: Solution for Fixed Effects of Total Score of Informant with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	3.6	0.36	<.001*
Mid-ECT VS Pre-ECT	-0.5	0.18	<.05*
Post-ECT VS Pre-ECT	-1.5	0.21	<.001*
Total number of ECT VS Pre-ECT	-0.03	0.03	0.43

* means statistically significant.

Table 26: Solution for Fixed Effects of Total Score of Attention with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	4.1	0.36	<.001*
Mid-ECT VS Pre-ECT	-0.4	0.15	0.01*
Post-ECT VS Pre-ECT	-0.4	0.19	0.03*
Total number of ECT VS Pre-ECT	-0.1	0.03	0.02*

* means statistically significant.

Table 27: Solution for Fixed Effects of Total Score of Autobiographical with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	5.1	0.33	<.001*
Mid-ECT VS Pre-ECT	-0.5	0.17	<.05*
Post-ECT VS Pre-ECT	-0.9	0.22	<.001*
Total number of ECT VS Pre-ECT	-0.1	0.03	<.05*

* means statistically significant.

Table 28: Solution for Fixed Effects of Total Score of Fund of Knowledge with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	4.6	0.25	<.001*
Mid-ECT VS Pre-ECT	-0.02	0.07	0.80
Post-ECT VS Pre-ECT	0.1	0.09	0.22
Total number of ECT VS Pre-ECT	<.01	0.02	0.97

* means statistically significant.

Table 29: Solution for Fixed Effects of Total Score of Recall with total number of ECT

Effect	Estimate	Standard Error	P-value*
Intercept	2.9	0.44	<.001*
Mid-ECT VS Pre-ECT	-0.6	0.26	0.02*
Post-ECT VS Pre-ECT	-0.5	0.22	0.04*
Total number of ECT VS Pre-ECT	-0.02	0.04	0.63

* means statistically significant.

Table 30: Solution for Fixed Effects of Total Score of ECCA with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	26.0	0.49	<.001*
Mid-ECT VS Pre-ECT	-2.4	0.59	<.001*
Post-ECT VS Pre-ECT	-3.5	0.61	<.001*
BL VS Pre-ECT	-0.3	0.09	<.05*

* means statistically significant.

Table 31: Solution for Fixed Effects of Total Score of MoCA with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	26.0	0.46	<.001*
Mid-ECT VS Pre-ECT	0.1	0.38	0.81
Post-ECT VS Pre-ECT	1.1	0.46	0.02*
BL VS Pre-ECT	-0.1	0.08	0.29

* means statistically significant.

Table 32: Solution for Fixed Effects of Total Score of Orientation with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	3.9	0.04	<.001*
Mid-ECT VS Pre-ECT	-0.02	0.05	0.74
Post-ECT VS Pre-ECT	-0.02	0.05	0.74
BL VS Pre-ECT	<.01	<.01	0.87

* means statistically significant.

Table 33: Solution for Fixed Effects of Total Score of Subjective with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	3.2	0.15	<.001*
Mid-ECT VS Pre-ECT	<.001	0.16	1
Post-ECT VS Pre-ECT	-0.5	0.17	<.05*
BL VS Pre-ECT	-0.1	0.03	<.001*

* means statistically significant.

Table 34: Solution for Fixed Effects of Total Score of Informant with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	3.6	0.14	<.001*
Mid-ECT VS Pre-ECT	-0.5	0.18	<.05*
Post-ECT VS Pre-ECT	-1.5	0.21	<.001*
BL VS Pre-ECT	-0.1	0.02	<.001*

* means statistically significant.

Table 35: Solution for Fixed Effects of Total Score of Attention with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	3.4	0.15	<.001*
Mid-ECT VS Pre-ECT	-0.4	0.15	<.05*
Post-ECT VS Pre-ECT	-0.4	0.19	<.05*
BL VS Pre-ECT	-0.03	0.03	0.24

* means statistically significant.

Table 36: Solution for Fixed Effects of Total Score of Autobiographical with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	4.6	0.13	<.001*
Mid-ECT VS Pre-ECT	-0.5	0.17	<.05*
Post-ECT VS Pre-ECT	-0.9	0.22	<.001*
BL VS Pre-ECT	-0.05	0.02	0.06

* means statistically significant.

Table 37: Solution for Fixed Effects of Total Score of Fund of Knowledge with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	4.6	0.11	<.001*
Mid-ECT VS Pre-ECT	-0.02	0.07	0.80
Post-ECT VS Pre-ECT	0.1	0.09	0.22
BL VS Pre-ECT	<.01	0.02	0.67

* means statistically significant.

Table 38: Solution for Fixed Effects of Total Score of Fund of Knowledge with number of BL

Effect	Estimate	Standard Error	P-value*
Intercept	2.8	0.20	<.001*
Mid-ECT VS Pre-ECT	-0.6	0.26	0.02
Post-ECT VS Pre-ECT	-0.47	0.22	0.04*
BL VS Pre-ECT	-0.1	0.03	0.07

* means statistically significant.